

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

FEB 26 2007

REMARKS

The following remarks address rejections and comments made by the Examiner in the Final Office Action mailed August 25, 2006. Claims 1 and 3-24 are currently pending. Claims 25-27 were previously withdrawn. Claim 2 was previously cancelled without prejudice. Claims 1, 19, 23 and 24 are currently amended. Amendments to claims 1, 19, 23 and 24 are supported throughout the specification, and specifically at page 5, lines 24-30; page 14, line 24 to page 15, line 2; pages 18-19; and original claim 23. With the above additions and amendments to the claims, no new matter has been added. Applicants respectfully request reconsideration of the present case in view of the following remarks.

Preliminary Amendments

Applicants thank the Examiner for the acknowledgement of the amendment to the Specification, and for acknowledgment of the receipt of a copy of the preliminary amendment filed on November 26, 2003.

Interview Summary

On June 14, 2006, a telephonic interview was conducted by Mark Skoog and Hema Viswanathan with Examiner Crow and Primary Examiner B.J. Forman. Applicants acknowledge receipt of the Interview Summary mailed June 21, 2006, and thank the Examiner for the same.

Rejection under 35 U.S.C. §102

Claims 1, 5, 6, 9, 12, 14, 15, 16 and 18 were rejected under 35 U.S.C. § 102(b) as anticipated by Sambrook et al. *Molecular Cloning, A Laboratory Manual*, 2nd ed., pages 7.12-7.15 and 7.26-7.29. Applicants respectfully traverse this rejection.

Applicants note that claim 1 is currently amended. As amended, the claim recite contacting the RNA-containing precipitate with a polymeric membrane having particle retention of up to about 10 μm , and wherein the polymeric membrane acts as a passive physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification.

The Examiner concedes that the Sambrook reference teaches a method for isolating RNA from previously purified total cytoplasmic RNA by affinity chromatography, using oligo(dT)-

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

cellulose membranes as affinity columns (*see* Office Action, page 3, paragraph 2). This is not the same as the method for RNA isolation recited in claim 1, where the polymeric membrane used to separate the RNA comprises a polymeric membrane that plays a passive role and acts as a physical barrier to the precipitate and retains the precipitate for purification.

The Sambrook reference teaches a paper that is derivatized with nucleic acid residues, and RNA is isolated by binding the RNA to the nucleic acid residues on the polymeric membrane. The Examiner concedes that Sambrook discloses use of Amersham Hybond mAP paper filters for isolation of RNA, i.e. filters that comprise poly-U residues bound to arylamine-substituted cellulose paper (*see* Utermohlen, at col. 3, ll. 30-36). In contrast, the polymeric membranes of the present invention are not described as derivatized with nucleic acid moieties or other molecules for increasing RNA-binding affinity. In fact, the disclosure teaches that RNA recovery is varied by altering the polymeric material used, or by varying the membrane pore size, but the disclosure does not state that the polymeric membranes are derivatized with nucleic acid moieties to enable RNA recovery. The Sambrook reference does not disclose the use of polymeric membranes having particle retention of up to about 10 μm .

For at least the above reasons, Applicants submit that the Sambrook reference does not teach all the limitations of claim 1. Claims 5, 6, 9, 12, 14, 15, 16, and 18 depend from claim 1, and therefore include the limitations of claim 1. In view of the amendment to claim 1 and the above remarks, Applicants respectfully request withdrawal of the rejection and reconsideration of claims.

Rejections under 35 U.S.C. §103

1. Claims 1, 4-10, 12-21 and 23 are rejected under 35 U.S.C. §103 as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook. Applicants respectfully traverse the rejection.

To make a *prima facie* case of obviousness, three criteria must be met. There must be (i) a teaching or suggestion in the cited references to modify the references or combine the teachings of the references; (ii) a reasonable expectation of success, and (iii) a teaching or suggestion of all the claim limitations on a cited reference, or combination of reference. *See In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner has the burden to establish a *prima facie*

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

case of obviousness. The mere fact that references can be combined does not render a claimed invention obvious unless the cited art suggests the desirability of the combination. *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990). Furthermore, the Examiner cannot rely on the skill in the art to provide the suggestion to combine references, unless such a suggestion appears in the cited references. *Al-Site Corp. v. VSI Int'l, Inc.*, 174 F.3d 1308 (Fed. Cir. 1999). If an independent claim is nonobvious, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

Independent claims 1 and 19, as amended, are directed to methods for preparing an RNA sample free of genomic DNA, wherein at least one step involves contacting an RNA-containing precipitate with a polymeric membrane that has particle retention of up to about 10 μ m. As amended, the claims recite that the polymeric membrane acts as a passive physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification.

The Colpan reference discloses general methods for purification of nucleic acids, but does not teach or otherwise suggest segregation of specific types of nucleic acids, i.e. separation of plasmid or genomic DNA from RNA. In fact, the Examiner concedes that the Colpan reference is "silent with respect to an RNA isolation membrane column." (*see* Office Action, page 6, paragraph 2). In addition, the Colpan reference is directed to use of a mineral substrate, and not a polymeric membrane and the pore sizes of the mineral substrate are much smaller than as claimed in the present Application.

The Examiner cites the Sambrook reference, for the disclosure of a column used to isolate RNA. As noted by the Examiner, Sambrook teaches isolation of nucleic acids using oligo(dT)-cellulose type affinity chromatography (*see* Office Action, page 6, paragraph 4). As described by Utermohlen, poly(A)+ RNA from total cytoplasmic RNA via binding of RNA to poly(U) residues bound to an arylamine-substituted cellulose paper membrane (*see* Utermohlen, at col. 3, ll. 30-36). Applicants submit that neither the Colpan nor Sambrook references teaches an RNA isolation method as recited in claims 1 and 19, where the mechanism of separation is precipitation, and where the RNA is isolated by means of a polymeric membrane that acts as a passive physical barrier (rather than an affinity column) for the precipitate, and retains the precipitate on the membrane for purification.

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

The cited references, taken alone, or in combination, fail to teach all the limitations of claims 1 and 19. Therefore, the Examiner has not established a *prima facie* case of obviousness and Applicants respectfully request withdrawal of the rejection and reconsideration of the claims. Furthermore, claims 4–10 and 12–18 depend from claim 1, and claims 20–21 and 23 depend from claim 19. These claims include all the limitations of independent claims 1 and 19, and therefore, no *prima facie* case of obviousness has been made with respect to these claims. For at least the foregoing reasons, Applicants submit that the claims are not obvious over the cited references, and respectfully request withdrawal of the rejection and reconsideration of the claims.

Furthermore, the Examiner has not established motivation to combine the cited references. The Colpan reference is directed to methods of purification using a mineral substrate. The Sambrook reference describes a method of isolating RNA from cytoplasm, using affinity chromatography (i.e. oligo-dT chromatography). The methods disclosed in the Colpan reference are not directed to separating one type of nucleic acid from a different type, but generally to isolation of nucleic acids from a biological sample. A person of skill in the art would not be motivated to combine the methods of the Colpan reference with those taught in the Sambrook reference, because the methods taught in the Colpan reference do not provide for separation of different types of nucleic acids from one another.

Therefore, Applicants submit the Examiner has not established a motivation to combine the references, and therefore, no *prima facie* case of obviousness has been made. For at least the foregoing reasons, Applicants submit that the claims are not obvious over the cited references, and respectfully request withdrawal of the rejection and reconsideration of the claims.

2. Claims 19, 21 and 22 are rejected under 35 U.S.C. §103(a) as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook, as evidenced by the Aldrich catalog.

Independent claim 19 recites isolation of RNA by precipitation using an RNA isolation column comprising a polymeric membrane that acts as a passive physical barrier for the precipitate and retains the precipitate for purification. As indicated in the foregoing remarks, neither the Colpan nor Sambrook references teach all the elements of claim 19, and therefore, the

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

Examiner has not established a case of *prima facie* obviousness. Applicants respectfully request withdrawal of the rejection.

Claims 21 and 22 depend from claim 19 and include all the limitations thereof. Neither the Colpan nor Sambrook references teach an isolation of RNA by contacting a polymeric membrane that acts as a passive physical barrier. With respect to claim 21, the Examiner contends that the Colpan reference teaches borosilicate glass fiber material with thickness of 50 to 2000 microns. Applicants respectfully disagree. The Colpan reference discloses the use of hollow bodies, such as commercially available tubes of polyethylene or polypropylene, with attached layers of silica gel, glass or quartz fibers with pore sizes of less than 5 microns (*see* Colpan, at col. 6, ll. 44-55) on which nucleic acids can be adsorbed. Applicants submit that the Colpan reference does not teach or suggest the use of a pre-filtration column comprising glass or borosilicate fibers with fiber thickness of 50 to 2000 microns, as recited in claim 21. The cited references, taken alone or in combination, do not recite all the limitations of claim 21, and therefore, a case of *prima facie* obviousness has not been made. Applicants respectfully request withdrawal of the rejection.

Claim 22 recites the method of claim 19, wherein the fiber material has a specific weight ranging from about 75 g/m² to about 300 g/m². The Examiner concedes that neither the Colpan nor Sambrook references teach the specific weights of the fiber material (*see* Office Action, at page 13, paragraph 2). Instead, the Examiner relies on the disclosure of the Aldrich catalog to provide the fiber weight limitation recited in claim 22. As indicated above, claim 22 includes all the limitations of claim 19. The Aldrich catalog, taken alone or in combination with the Colpan and Sambrook references, does not teach an RNA isolation column comprising a polymeric membrane that acts as a passive physical barrier to the precipitate.

With respect to claim 22, Applicants respectfully disagree that the Aldrich catalog teaches fiber weights as recited in the present claims. The Aldrich catalog discloses fiber glass wool made from fine borosilicate fibers with pore size of 8 microns. The fiber glass wool is provided in woven roving approximately 2 inches in diameter and 22 feet in length, with a weight of 454 g per package. The Examiner uses these dimensions to calculate a possible specific weight for the fiber glass wool disclosed in the Aldrich catalog. In these calculations, the Examiner assumes a filter layer thickness (i.e. length) of 0.25 inches (*see* Office Action, at page

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

13, paragraph 3). However, this filter layer thickness is not recited in the present claims or provided in the present specification. Furthermore, Applicants submit that a fiber layer thickness of 0.25 inches is not inherently disclosed in the Aldrich catalog. The Aldrich catalog specifies only a total length of 22 feet for the entire glass wool fiber bundle. As different applications would require fiber layers of different thickness, a person of skill in the art would not assume the layer thickness suggested by the Examiner, based on the disclosure in the Aldrich catalog. Therefore, as the Aldrich catalog does not teach fibers with specific weight of about 75 g/m² to about 300 g/m², all the limitations of claim 22 have not been taught or suggested in the cited references. Applicants respectfully request withdrawal of the rejection.

3. Claims 1, 3, 19, and 24 are rejected under 35 U.S.C. §103(a) as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook in further view of Utermohlen (U.S. Patent No. 5,437,976). Applicants respectfully traverse the rejection.

As indicated above, independent claims 1 and 19, as amended, are directed to methods for preparing an RNA sample free of genomic DNA, wherein at least one step involves contacting a polymeric membrane with an RNA-containing precipitate. As amended, the claims recite a polymeric membrane that acts as a passive physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification.

As indicated above, neither the Colpan nor Sambrook references teaches an RNA isolation method as recited in claims 1 and 19, where the mechanism of separation is precipitation, and where the RNA is isolated by a polymeric membrane that acts as a passive physical barrier (rather than an affinity column) for the precipitate, and retains the precipitate on the membrane for purification.

With respect to claims 3 and 24, the Examiner concedes that neither the Colpan nor Sambrook references teach or suggest a nylon membrane, but relies on the Utermohlen reference for this limitation. Applicants submit that the Utermohlen reference does not overcome the shortcomings of the Colpan and Sambrook references. As noted by the Examiner, the Utermohlen reference teaches mRNA affinity chromatography using woven nylon matrices attached to poly(dT) moieties (see Utermohlen, col. 5, ll. 52-59 and Abstract, ll. 3-5). However,

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

the reference does not teach a polymeric membrane that acts as a passive physical barrier for a precipitate.

Therefore, as the cited references, taken alone or in combination, do not teach or suggest all the limitations of the claims, a *prima facie* case of obviousness has not been made. Applicants respectfully request withdrawal of the rejection and reconsideration of the claims.

4. Claims 1 and 11 are rejected under 35 U.S.C. §103 as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook, in further view of Crossway (U.S. Patent No. 4,996,144). Applicants respectfully traverse the rejection.

The arguments and remarks provided above are also fully relevant here and are incorporated by reference to avoid repetition. To briefly summarize, the combination of the Colpan and Sambrook references fails to teach all the elements of claim 1. Specifically, neither reference, either alone or in combination, discloses contacting a polymeric membrane with an RNA-containing precipitate, where the polymeric membrane that acts as a passive physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification.

With respect to claim 11, the Examiner concedes that the Colpan and Sambrook references do not teach or suggest digestion with DNase after isolation of the RNA-containing precipitate. Instead, the Examiner cites the Crossway reference for a method of purifying nucleic acids using digestion with DNase (see Crossway, at col. 5, ll. 61-67). Applicants respectfully submit that the Crossway reference provides only a general method for digestion with DNase to provide a sample where RNA can be detected. The Crossway reference, taken alone or in combination with the other cited references, does not disclose or suggest a method for digesting an RNA-containing precipitate with DNase, where the RNA-containing precipitate is contacted with a polymeric membrane that acts as a passive physical barrier to the precipitate.

Applicants assert that the cited references, taken alone, or in combination with each other, fail to teach all the limitations of the present claims. Therefore, the Examiner has not established a *prima facie* case of obviousness and the Applicants respectfully request withdrawal of the rejection and reconsideration of the claims.

Appl. No. 10/693,428
Amendment dated February 26, 2007
Reply to Advisory Action of January 22, 2007

Provisional Obviousness-type Double Patenting

Claims 1 and 3 were provisionally rejected for nonstatutory obviousness-type double patenting over claims 1-3 of copending Application No. 10/804,938 in view of the Sambrook reference. Claims 19-22 are provisionally rejected for nonstatutory obviousness-type double patenting over claims 1-3 of copending Application No. 10/914,920 in view of the Sambrook reference.

Without acquiescing to the above rejections, Applicants defer entry of a terminal disclaimer, if determined necessary, to a time when either the present application or one of the above copending applications has been allowed.

Interview Request

Applicants respectfully request the Examiner for a telephone interview on receipt of this paper.

SUMMARY

Favorable consideration and entry of these amendments are respectfully requested. The Examiner is encouraged to contact the undersigned attorney with any questions regarding this application.

Respectfully submitted,
MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903
(612) 332-5300

Date: February 26, 2007

KMK:HLV:dc

Katherine M. Kowalchuk
Katherine M. Kowalchuk
Reg. No. 36,848